

### Remarks

Claims 1-58 are pending in this application. Claims 1-9, 17-44, 47-53, 57 and 58 have been withdrawn from consideration. Claims 10-16, 45, 46 and 54-56 are rejected.

### ELECTION/RESTRICTIONS

The Examiner states in part:

The specification recites a number of nucleic acid sequences that are not properly identified with sequence identifiers (see for example, p. 39 of specification, and throughout, and also at least figures 1, 2A, and 2B). In order to comply with the requirements of the sequence rules (37 CFR 1.821 – 1.825), Applicant must submit, as appropriate, a new CRF and paper copy of the Sequence Listing containing these sequences, in addition to the previously listed sequences, an amendment directing entry of the Sequence Listing into the specification, an amendment directing the insertion of the SEQ ID NOs into the appropriate pages of the specification and a letter stating that the content of the paper and computer readable copies are the same.

*PTO Paper* dated May 15, 2003 at 2-3.

Applicants respectfully request that the "new" Sequence Listing submitted with this amendment be entered into the specification.

Applicants have amended the specification to properly identify nucleic acid sequences with sequence identifiers. For the figures (Figs. 1, 2A and 2B), Applicants have inserted the sequence identifier in the "BRIEF DESCRIPTION OF THE DRAWINGS" section.

Applicants are submitting, the following items:

- (a) a new CRF and paper copy of the sequence listing containing the sequences, in addition to the previously listed sequences;
- (b) an amendment directing the entry of the sequence listing into the specification (see *supra*);
- (c) an amendment directing the insertion of the SEQ ID NOs. into the appropriate pages of the specification (See "Amendments to the Specification"); and

- (d) a letter stating that the content of the paper and computer readable form are the same.

### SPECIFICATION

The Examiner states:

The disclosure is objected to because of the following informalities:  
The specification refers to Figure 1 on page 38, but the figure being referred to within the text of the specification does not seem to be the same figure 1 as is present in the drawings. Page 42 also refers to Figure 1. Likewise, page 45 refers to a Figure 2 but does not appear to be referring to the Figure 2 present in this application.

*Id.* at 3.

Applicants have amended the specification so that the specification refers to the correct figures, thus alleviating this objection.

### INFORMATION DISCLOSURE STATEMENT

The Examiner states:

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the Examiner on form PTO-892, they have not been considered.

*Id.* at 3.

Applicants acknowledge the Examiner's statement regarding references considered by the Examiner.

### CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 10-16, 45, 46, 54, 55, and 56 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

The Examiner states:

Claim 10 is indefinite because the preamble recites the method is for screening animals to determine those more likely to exhibit improved meat quality traits, but the method steps recite steps of assaying a biological sample for the presence of a genotype. The claim does not set forth which of the recited genotypes for positions 199 and 200 is in fact associated with improved meat quality traits. Claims 11-16 are indefinite for reasons as they depend from claim 10.

*Id.* at 4.

Applicants have amended the preamble of claim 10 to match the remainder of the claim according to the Examiner's suggestions. Also, claim 10 has been amended to recite which genotype for positions 199 and 200 are associated with specific meat quality traits such as color, pH level, marbling, and drip loss. Claims 11-16 by their dependency to independent claim 10 contain all the limitations of amended claim 10. Therefore, Applicants respectfully request the Examiner to withdraw this rejection.

The Examiner states:

Claims 10-16, 45, 46, 54, 55, and 56 are further indefinite over the recitation "improved meat quality traits" because whether or not a particular meat quality trait is an improvement is entirely a relative matter and thus, it is unclear what traits are being predicted by the methods.

*Id.*

Applicants have amended claim 10 to recite specific traits such as color, pH level, marbling, and drip loss, thereby making more clear what traits are being predicted by the methods. Support is found throughout the specification as filed. Claims 45, 46, 54, 55 and 56, have also been amended to recite specific traits, which are supported by the application as filed. Applicants respectfully request reconsideration of these claims and withdrawal of this rejection.

The Examiner states:

Claims 10-16, 45, 46, 54, 55, and 56 are indefinite because the recitation "said animal" in the assaying steps of the claims does not have proper antecedent basis in the claims because the claims do not previously refer to an animal but to animals.

*Id.* at 5.

Claims 10-16, 45, 46, 54, 55, and 56 have been amended to recite "an animal", thereby having proper antecedent basis in the claims. Applicants respectfully request this rejection be withdrawn.

The Examiner states:

Claims 10-16 are indefinite over the recitation that the "genotype" to be determined is characterized by "a polymorphism" in claim 10. This is confusing because a genotype is generally accepted to be a recitation of particular alleles present at a polymorphic site in a nucleic acid, yet in claim 10 the genotype is characterized by the presence of the polymorphism itself, regardless of the allele present at the particular positions in the PRKAG3 gene.

*Id.*

Claim 10 has been amended to more clearly describe the invention by reciting in part "a method of screening animals for a genotype associated with litter size and meat quality traits such as color, pH level, marbling, and drip loss, comprising obtaining a biological sample of material from an animal; and assaying said sample for a PRKAG3 genotype comprising at least one polymorphic allele, wherein said PRKAG3 genotype encodes a polypeptide having at least 95% sequence identity to SEQ ID NO:2, and is characterized by a nucleic acid sequence which encodes a polypeptide having an amino acid of valine at position 199 and arginine at position 200, or an isoleucine at position 199 when an arginine is at position 200 in SEQ ID NO:2", thereby reciting particular alleles present at a polymorphic site in the encoded gene product. Claims 11-16, by virtue of their dependency contain all the limitation of amended independent claim 10. Applicants request this rejection be withdrawn.

The Examiner states:

Claims 10-16 are indefinite over the recitation "or its equivalent" in claims 10 because neither the specification nor the claims set forth or explain what makes a position an equivalent position. That is, it is unclear how to determine or what constitutes the equivalent position. Claim 10 sets forth that the equivalent is determined by a BLAST comparison to determine the equivalent of the polymorphic position in other PRKAG3 polypeptides. Claim 11 is indefinite for reciting "or its equivalent" for the same reasons as claim 10.

*Id.* at 6.

Applicants have amended claim 10 recite that the polymorphic allele includes an isolated polypeptide that exhibits substantial sequence identity to SEQ ID NO:2 when said polypeptide is aligned with SEQ ID NO:2 in a Blast comparison using default parameters. Support is found in the specification as filed (see spec. pages 9-15). Such sequence alignment programs are known to those of ordinary skill in the art. Moreover, the specification discloses on page 10, for example, that the Blast comparisons may be used to ascertain whether the particular allele is analogous to the one disclosed herein. (See page 10 and on in specification). Applicants have amended claim 11 to recite "the method of claim 10 wherein said polymorphism is a transition of a guanine to an adenine at nucleotide position 595 of SEQ ID NO:1 or a nucleotide sequence having substantial sequence similarity to SEQ ID NO:1 as measured using BLAST sequence comparison algorithm" thereby setting forth what makes a position an equivalent position.

The Examiner states:

Claim 11 is indefinite over the recitation of "at nucleotide position 595" because the claim fails to provide a reference sequence for which position 595 is relevant. Use of a sequence identifier to set forth the position would overcome this rejection.

*Id.*

Claim 11 has been amended to recite a sequence identifier to set forth the position.

The Examiner states:

Claims 12-13 are indefinite because it is unclear how or why one would use a short interspersed element polymorphism test, which is designed to detect SINE elements, to detect a single nucleotide polymorphism as is being detected in claim 12.

*Id.*

Although not acceding to the Examiner's rejection, claims 12 and 13 have been cancelled.

The Examiner states:

Claim 13 is indefinite because it is unclear what is meant for a primer to be "selected from and based upon" and further because the designators "RP1F" and "PN52R2" are arbitrary identifiers and it is unclear what these designations mean. Use of sequence identifiers is recommended.

*Id.*

Although not acceding to the Examiner's rejection, Applicants have cancelled claim 13.

The Examiner states:

Claim 16 is indefinite because it is unclear what is meant for a primer to be "selected from and based upon" and further because the designators "RNF" and "RNR" are arbitrary identifiers and it is unclear what these designations mean. Use of sequence identifiers is recommended.

*Id.*

Applicants have amended claim 16 to recite "primers selected from the group consisting of SEQ ID NO:16 and SEQ ID NO:23", thus using sequence identifiers. Although not acceding to the Examiner's rejections, Applicants have deleted the recitation "selected from and based upon".

The Examiner states:

Claim 45 is indefinite over the recitation that the "genotype" to be determined is characterized by particular amino acids. This is confusing because the genotype is being determined for a genetic sample, yet the claim recites assaying for the presence of amino acids. Further, the claim does not set forth an identification for what protein the amino acid positions are imbedded within, and thus the recitation of particular positions recited in the claim are completely arbitrary. Also, the claim fails to set forth method steps of how the purpose of the claim as recited in the preamble is accomplished.

*Id.* at 7.

Applicants have amended claim 45 to recite in part "assaying the PRKAG3 protein as depicted in SEQ ID NO:2 in said sample for the presence of a threonine at amino acid position 30, a glycine at amino acid position 52 and an isoleucine at amino acid position 199 in SEQ ID NO:2, wherein the presence of said threonine at amino acid position 20, glycine at amino acid position 52 and isoleucine at amino acid position 199 is indicative of said animal possessing favorable meat quality traits comprising color, pH level, marbling, and drip loss, wherein said animal possesses at least 90% sequence identity to SEQ ID NO:2", thereby reciting that the genotype is determined from a from a "biological" sample, i.e., protein, setting forth an identification for what protein the amino acid positions are imbedded within, and setting forth method steps of how the purpose of the claim as recited in the preamble is accomplished.

The Examiner states:

Claim 46 is indefinite over the recitation that the "genotype" to be determined is characterized by a particular amino acids. This is confusing because the genotype is being determined for a genetic sample, yet the claim recites assaying for the presence of amino acids. Further the claim does not set forth an identification for what protein the amino acid positions are imbedded within, and thus the recitation of a particular position recited in the claim is completely arbitrary. Furthermore, the claim is indefinite because it fails to set forth in the method steps how the purpose of the claim as recited in the preamble is accomplished. That is, the claim fails to set forth how assaying for the presence of a genotype results in determining an animal more likely to have favorable meat quality traits.

*Id.*

Claim 46 has been amended to recite in part, "assaying the PRKAG3 protein as depicted in SEQ ID NO:2 in said sample for the presence of a isoleucine at position 199 and an arginine at position 200, wherein the presence of said isoleucine at position 199 and arginine at position 200 is indicative of an animal having a lower level of glycogen, lactate, and glycolytic potential,

higher ham and loin pH and favorable color scores", thereby reciting that the genotype is determined from a from a "biological" sample, i.e., protein, setting forth an identification for what protein the amino acid positions are imbedded within, and reciting method steps of how assaying for the presence of a genotype results in determining an animal more likely to have favorable meat quality traits.

The Examiner states:

Claims 54 and 55 are indefinite because they fail to set forth in the method steps how the purpose of the claims as recited in the preamble is accomplished. That is, the claim fails to set forth how assaying for the presence of a genotype results in determining an animal more likely to have favorable meat quality traits. Furthermore, the term "the PRKAG3" in the last line of the claims lack proper antecedent basis in the claims.

*Id.* at 7-8.

Claims 54 and 55 have been amended to recite how the purpose of the claim as recited in the preamble is accomplished. Moreover the claims have been amended to provide proper antecedent basis for the term "the PRKAG3".

The Examiner states:

Claim 56 is indefinite over the recitation that the "genotype" to be determined is characterized by particular amino acids. This is confusing first, because the genotype is being determined for a genetic sample, yet the claim recites assaying for the presence of amino acids. Further, the claim does not set forth an identification for what protein the amino acid positions are imbedded within and thus the recitation of particular positions recited in the claim are completely arbitrary. Furthermore, the claim is indefinite because it fails to set forth in the method steps how the purpose of the claim as recited in the preamble is accomplished.

*Id.* at 8.

Claim 56 has been amended to more clearly describe the invention by reciting in part, "a method of screening animals to determine those more likely to have favorable meat quality traits comprising obtaining a sample of biological material from an animal; and isolating PRKAG3



protein from said biological material; assaying for the presence of amino acid changes in said animal which are associated with favorable meat quality traits comprising color, pH level, marbling, and drip loss, said amino acid changes are characterized by a threonine at amino acid position 30, a serine at amino acid position 52 and a valine at amino acid position 199 in PRKAG3 protein as depicted in SEQ ID NO:2.

**35 U.S.C. § 112, FIRST PARAGRAPH**

Claims 10-16, 45, 46, 54, 55, and 56 were rejected under 35 U.S.C. § 112, first paragraph.

The Examiner states in part:

The specification does not reasonably provide enablement for methods which screen any possible animal for the same predispositions or methods which look at genes other than the PRKAG3 gene or methods which utilize polymorphisms or haplotypes other than those specifically indicated as being supported by enabling disclosure or methods which predict an increased likelihood of any and all favorable meat quality trait. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

*Id.* at 8-19.

Applicants have amended claims 10-16, 45, 46, 54, 55, and 56 to recite that the animal has at least 90% sequence identity relative to a protein denoted with a sequence identifier.

Applicants submit that due to the highly conserved nature of this protein, it is expected that other animals will demonstrate polymorphisms in this protein or a region thereof which are analogous to those disclosed and claimed which can be determined by sequence homology or similar protein effects. Methods such as hybridization, which are well known in this art, can be used to identify polypeptide sequences having substantial sequence similarity to the sequence of the invention without undue experimentation. In the lab, hybridization conditions would enable one skilled in the art to detect a polypeptide having at least 90% or 95% sequence identity because

such conditions would reasonably ensure having high complementarity to SEQ ID NO:2 and its naturally occurring variants.

### PRIORITY

The Examiner states:

Although the Applicants' claim for domestic priority under 35 U.S.C. § 119(e) is acknowledged, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. § 112 for claims 10-16, 45, 46, 54, 55, and 56 of this application. None of these provisional applications provide adequate support under 112 first paragraph for the claims to their full scope for at least the same reasons why the instant specification does not provide adequate support for the claims. Furthermore, the Examiner states none of the provisional applications provides support for the methods which examine particular haplotypes since these provisional applications do not provide analysis of the relationship between meat quality traits and any particular haplotypes. Thus, the filing date for the elected claims is considered to be the instant filing date, September 10, 2001.

*Id.* at 19.

Applicants traverse. Applicants respectfully submit that the provisional applications provide adequate support under 112, 1<sup>st</sup> paragraph for the claims to their full scope. In U.S. Provisional Serial No. 60/299,111, Applicants disclose on page 35, first paragraph, haplotypes associated with a trait(s).

### CLAIM REJECTIONS - 35 U.S.C. § 102

Claims 10-16, 45, 46, 54, and 55 were rejected under 35 U.S.C. § 102(a) or 102(b) as being anticipated by Milan et al. (*Science*, 19 May 2000, Vol. 288, pages 1248-1251).

The Examiner states:

Milan et al. teach[es] a method for screening animals to determine those more likely to exhibit improved meat quality traits comprising: obtaining a biological sample of material from an animal (p. 1249); and assaying for the presence of a genotype characterized by a polymorphism in the PRKAG3 gene characterized by an amino acid of valine at position 199 and an amino acid of arginine at position 200 (Table 1, alleles 2-4) OR an isoleucine at position 199 and an arginine at position 200 (Table 1, allele 5). Specifically, Milan et al. teach that animals with their alleles 2-5 have higher meat quality (as indicated by their having the *rn+* allele). Furthermore, Milan et al. teach a method wherein they detect threonine at amino acid position 30, a glycine at amino acid 52 and an isoleucine at amino acid position 199. Such detection takes place in their allele 5 which is an allele from *rn+* pigs. In all of the alleles detected by Milan et al., a glycine was encoded at amino acid 52 (see Fig. 2), and thus the detection of such a nucleic acid encoding the amino acids recited in claim 45 is inherent in the methods taught by Milan et al.

*Id.* at 20-21.

A prior art patent, publication, or event is for the same "invention", as that word is used in §102, and therefore anticipating, if the prior art patent, publication, or event discloses each and every limitation found in the claims, either expressly or inherently. *Rockwell Intern. Corp. v. U.S.*, 147 F.3d 1358, 1363 (Fed. Cir. 1998). Each claim limitation must be found in a single prior art references. Applicants respectfully submit that Milan does not disclose the same invention as Applicants, therefore does not anticipate. Milan et al. shows that the 200Q variant (*RN*<sup>-</sup>) is always found with 199V. However, 199V is found with both 200R and 200Q and 199I is always found with 200R. Milan discloses that only the R200Q substitution was exclusively associated with *RN*<sup>-</sup> (See Milan page 149, col. 1, last para. and Fig. 2C). The 200Q allele was found in all *RN*<sup>-</sup> animals but not in any *rn*<sup>+</sup> animals from Hampshire or other breeds. (*Id.* at col. 3 and Table 2). Milan discloses that this is consistent with the assumption that *RN*<sup>-</sup> originated in the Hampshire breed. Milan et al. merely discloses the sequence of the PRKAG3 and some polymorphisms for the gene indicating that the mutation at position 200 is causative for a major gene effect known as *RN*<sup>-</sup>. However, Milan et al. does not disclose any evidence for any other

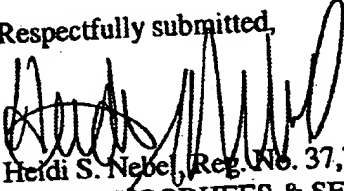
possible effect of polymorphism or variation in this gene and variation in traits of interest as disclosed by Applicants. Prior to Applicants' invention, there was no evidence for this gene influencing economic traits in other breeds. Conversely, Applicants disclose the presence of new economically important alleles of the PRKAG3 gene affecting glycogen content in muscle and in general meat quality traits of pigs which include color, pH level, marbling, and drip loss and also the trait litter size. (See spec. page 18). Therefore, Applicants' invention is not anticipated because Applicants disclose that there is variation for meat quality due to PRKAG3 in animals that are m<sup>+</sup>. (See spec. page 36, Example 1 under "Abstract"). Additionally, Applicants provide evidence that there was variation for glycolytic potential, the trait normally associated with RN<sup>-</sup> in lines that do not segregate for RN<sup>-</sup>. (See in general Example 1 and page 41 under "Results").

Additionally, Applicants are herein submitting for consideration, the declaration of Dr. Max F. Rothschild under 37 C.F.R. § 1.131, to overcome Milan et al.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

  
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